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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/619,290	07/19/2000	Robert Sackstein	0152.00378	2235

7590 03/24/2004

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EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 03/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)
	09/619,290	SACKSTEIN ET AL.
	Examiner	Art Unit
	Phillip Gambel	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *26 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *5-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4)☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____.

DETAILED ACTION

1. Applicant's election without traverse of Invention I (claims 1-4) on 1/26/04 is acknowledged.

Claims 5-29 are withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-4 are being considered in the instant application.

2. The filing date of the instant claims is deemed to be the filing date of instant application USSN 09/619,290, i.e. 7/19/2000.

It is noted that priority applications do not appear to provide sufficient written description of:

"An isolated and purified glycoprotein and functional analogues thereof characterized by being expressed on at least primitive hematopoietic cells; being a ligand for L-selectin *or E-selectin*; the binding of the ligand to L-selectin or E-selectin being inhibited by anti-CD34 antibodies".

Priority applications do not appear to provide written support for the limitations relying upon the recitation of "E-selectin" in defining the claimed "glycoprotein and functional analogues" in the instant claims

If applicant desires priority prior to 7/19/2000, applicant is invited to point out and provide documentary support for the priority of the instant claims.
Applicant is reminded that such priority for the instant limitations requires written description and enablement under 35 U.S.C. § 112, first paragraph.

2. Applicant should amend the first line of the specification to update the status of the priority documents.

3. Applicant's request for a response to the objections to the drawings to be held in abeyance on 1/26/04 is acknowledged.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim 1, line 5 is objected to because "E-selecting" should be "E-selectin" as the correct spelling.

Appropriate corrections are required

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification broadly describes and the claims recite as part of the invention the following:

"An isolated and purified glycoprotein and functional analogues thereof characterized by being expressed on at least primitive hematopoietic cells; being a ligand for L-selectin or E-selectin; the binding of the ligand to L-selectin or E-selectin being inhibited by anti-CD34 antibodies; being resistant to O-sialogylcoprotein endopeptidase activity; being unrecognized by MECA-79 a monoclonal antibody which identifies ligands of L-selectin on lymph node high endothelial venules; and being sulfation-independent" "and functional analogues thereof".

Such "glycoprotein" and "functional analogues" do not meet the written description provision of 35 USC 112, first paragraph.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

Applicant relies upon identifying KG1a L-selectin ligand which binding activity is not sulfate-dependent utilizing an adherence assays; however applicant has not provided sufficient structural information that identifies a physiologic structure.

In addition, as indicated in Sackstein et al., Blood 89: 2773-2781, 1997 (1449; #77); applicant's own work acknowledges efforts are directed at isolating and characterizing the structure of the claimed KG1a L-selectin ligand (see entire document, including the Discussion). Here, it is noted that the structural features of the claimed KG1a L-selectin ligand remain to be determined

Also, Sackstein et al. notes that the structural determinants conferring L-selectin binding may vary in a cell and tissue-specific manner (see Abstract and Discussion); yet applicant has not provided such structural information.

Further, there is a lack of written description for "functional analogues"; given the absence of structural features that define the claimed "KG1a L-selectin ligand".

The specification as filed does not provide sufficient written description support for the claimed "KG1a L-selectin ligand" and "functional analogues thereof".

The skilled artisan cannot envision the claimed "L-selectin ligand" and "functional analogues thereof" in the absence of a detailed chemical structure of the "L-selectin ligand" and "functional analogues thereof" and therefore conception cannot be not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. Here, defining structural features are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

While actual reduction to practice is only one of several ways to satisfy the Written Description Requirement; The Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement make clear that if a claimed genus does not show actual reduction to practice for a representative number of species; then the Requirement may be alternatively met by reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001, see especially page 1106 3rd column).

In the absence of a nexus between structural and functional characteristics that are shared by members of the genus of L-selectin ligands and "functional analogues thereof" encompassed by the claimed invention, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. See University of California v. Eli Lilly and Co. 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Further, it appears that applicant has identified the hematopoietic cell L-selectin / E-selectin ligand (HCELL) are also referred to a KG1a CD44, which is a glycoform of CD44 and comprising SEQ ID NO:1 as set forth in Sackstein (US 2003/0040607 A1; see entire document, including Summary of the Invention, Examples, Table 1 and Claims)

In contrast there is insufficient written description that the instant "L-selectin ligand and functional analogues thereof" as a glycoform of CD44 or comprises a specific amino acid sequence (or encoded by a specific nucleic acid sequence) which encodes said claimed L-selectin ligand in the instant disclosure as filed.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

8. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

Applicant has not provided sufficient biochemical information (e.g. amino acid sequence) that distinctly identifies the claimed "KG1a L-selectin ligand" and "functional analogues thereof". While "being a ligand for L-selectin or E-selectin" may have some notion of the activity of the claimed glycoprotein and applicant has relied upon the property of being sulfation-independent as well as the combination of characteristics to distinguish the instant glycoprotein from other L-selectin or E-selectin ligands or "functional analogues thereof"; claiming biochemical molecules by certain functional attributes fails to enable the skilled artisan to make and use the claimed glycoprotein, without defining what the disclosed and claimed "KG1a L-/E-selectin ligand" is made up of. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

However, the precise structural features that direct binding activity for the claimed nonconventional L-/E-selectin ligand remains to be determined. The isolation and characterization of the structure of this molecule has not been set forth, therefore the scope of the claimed isolated and purified glycoproteins and functional analogs characterized by properties (a)-(e) cannot be ascertained. Again, the claimed and disclosed characteristics may have some notion of the activity of the glycoprotein as an adhesion molecule and a selectin ligand, there is insufficient precision in the claims which distinctly claims the isolated and purified glycoprotein and functional analogs thereof.

In addition, as indicated in Sackstein et al., Blood 89: 2773-2781, 1997 (1449: #77); applicant's own work acknowledges efforts are directed at isolating and characterizing the structure of the claimed KG1a L-/E- selectin ligand (see entire document, including the Discussion). Here, it is noted that the structural features of the claimed KG1a L-/E-selectin ligand remain to be determined after applicant's priority dates. Here, the post-filing date reference relies upon the same or nearly the same functional characterization as that disclosed in the specification as filed and acknowledges that the KG1a L-/E-selectin ligand has not been isolated and characterized to the point that the skilled artisan could make and use the claimed "L-/E-selectin glycoprotein" and " functional analogues thereof" as an L-/E-selectin ligand on primitive hemopoietic stem cells.

Here, Sackstein et al. acknowledges the existence and structural as well as functional attributes of known L-/E-selectin ligands in distinguishing the claimed/disclosed "KG1a L-selectin ligand" (see Introduction and Discussion).

Also, Sackstein et al. notes that the structural determinants conferring L-selectin binding may vary in a cell and tissue-specific manner (see Abstract and Discussion); yet applicant has not provided such structural information.

Further, it appears that applicant has identified the hematopoietic cell L-selectin / E-selectin ligand (HCELL) are also referred to a KG1a CD44, which is a glycoform of CD44 and comprising SEQ ID NO:1 as set forth in Sackstein (US 2003/0040607 A1; see entire document, including Summary of the Invention, Examples, Table 1 and Claims).

Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which changes can be tolerated in a polypeptide's amino acid sequence and still retain similar functionality (e.g. L-selectin ligand or E-selectin ligand) requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which a polypeptide's structure relates to its functional usefulness. However, the problem of predicting polypeptide structure from mere sequence data of a single amino acid sequence and in turn utilizing predicted structural determinations to ascertain binding or functional aspects KG1a L-/E-selectin analogs and finally what changes can be tolerated with respect thereto is complex and well outside the realm of routine experimentation.

In re Fisher, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

As pointed out herein, the specification as filed as well as a post-filing date reference has not provided sufficient structural or biochemical information to enable the skilled artisan to make and use the claimed KG1a L-selectin ligand. Further, it has been well known to those skilled in the art at the time the invention was made that minor structural differences among structurally related compounds or compositions can result in substantially different biological or pharmacological activities.

For example, Skolnick et al. (Trends in Biotech., 18(1):34-39, 2000) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2).

Because of the lack of sufficient guidance and predictability in determining which modifications would lead to "functional analogues" of the claimed/disclosed "KG1a L-/E-selectin ligand" and "analogues thereof" and that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) was not well understood and was not predictable (e.g. see Ngo et al., in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al., (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495.); it would require an undue amount of experimentation for one of skill in the art to arrive at enabling the "KG1a L-/E-selectin ligand and "functional analogues".

Without sufficient guidance, making and using the claimed "KG1a L-/E-selectin ligand" and "functional analogues" thereof, including cell- and tissue-specific L-selectin ligands is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

9. Claims 1-4 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

A) Claims 1-4: It is apparent that the MECA-79 antibody is required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line / hybridoma which produces this antibody. See 37 CFR 1.801-1.809.

In addition to the conditions under the Budapest Treaty, applicant is required to satisfy that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent in U.S. patent applications.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the original deposit is made after the effective filing date of an application for patent, the applicant should promptly submit a verified statement from a person in a position to corroborate the fact, and should state, that the biological material which is deposited is a biological material specifically identified in the application as filed, except if the person is an attorney or agent registered to practice before the Office, in which the case the statement need not be verified. See MPEP 1.804(b).

B) If applicant amends the claims to recite the KG1a cell line in the instant claims, applicant would be required to satisfy the enablement requirements of 35 USC 112, first paragraph, with a deposit of the KG1a cell line.

Claims 1-4: Upon consideration of the specification,; it appears that the "KG1a" cell line is required to practice the claimed invention. It appears that applicant has relied upon characterizing the "claimed KG1a L-selectin ligand" by functional screening of the KG1a cell line (see the instant specification). As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it is not so obtainable or available, the enablement requirements of 35 USC 112, first paragraph, may be satisfied by a deposit of the cell line. See 37 CFR 1.801-1.809.

C) Alternatively, applicant is invited to provide evidence that either the MECA-79 hybridoma or the KG1a cell line, if claimed, are / were publicly available.

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office Action:

> A person shall be entitled to a patent unless --
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 1-4 are rejected under 35 U.S.C. § 102(a)(b) as being anticipated by Sackstein et al. (Exptl. Hematol. 22: 788, 1994; Abstract 414).

Sackstein et al. teach the indication of a KG1a L-selectin ligand that appears to be the same L-selectin ligand claimed (see Abstract).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced KG1a L-selectin ligand.

Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

Given the ambiguity of the instant claims, this prior art rejection has been applied under 35 U.S.C. § 102(a)(b).

12. Claims 1-4 are rejected under 35 U.S.C. § 102(b) as being anticipated by Stamenkovic et al. (EMBO Journal 10: 343—348, 1991) (see entire document, including Figure 1) as evidenced by Sackstein (US 2003/0040607 A1).

Stamenkovic et al. teach hematopoietic and epithelial forms of CD44, including encoding nucleotide and amino acids of CD44, which appear to the same or nearly the same as the instant hematopoietic cell L-selectin / E-selectin ligand (HCELL) also referred to a KG1a CD44, which is a glycoform of CD44 and comprising SEQ ID NO:1 as set forth in US 2003/0040607 A1 (see entire document, including Summary of the Invention, Examples, Table 1 and Claims).

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced CD44 glycoproteins.

Products of identical chemical composition can not have mutually exclusive properties. A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present. In re Spada 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP 2112.01.

13. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

14. Claims 1-4 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of copending application USSN 10/042,421, as evidenced by Sackstein (US 2003/0040607 A1). Although the conflicting claims are not identical, they are not patentably distinct from each other because they are drawn to the same or nearly the same hematopoietic cell L-selectin / E-selectin ligands (HCELL) also referred to a KG1a CD44, which is a glycoform of CD44 and comprising SEQ ID NO:1 as set forth in Sackstein (US 2003/0040607 A1; see entire document, including Summary of the Invention, Examples, Table 1 and Claims).

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (571) 272-0844. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Phillip Gambel, PhD.
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March 15, 2004